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Forté White Paper

Forté Brain™

Science-based, Targeted Nutritional Support for Optimal Brain Health

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Nutrition and the Aging Brain

Aging is characterized by a gradual and progressive loss of function over time, with downstream effects on overall health and well-being. In addition to changes in body composition—including decreased bone density and lean body mass—many older adults display a slow decline in cognitive status, including impaired memory and other cerebral capacities.[1] In fact, mild cognitive impairment is present in approximately 16 percent of adults over the age of 70.[2] However, this impairment may not be solely due to age-related cognitive decline—it may be linked to nutritional insufficiencies that impact cognitive performance.

Nutrition plays a significant and crucial role in both short- and long-term brain health Recent research has highlighted the potential impact of nutritional factors and individual micronutrients on the brain, cognitive performance, and even the development of Alzheimer's disease, the most common form of dementia.[3] In fact, measures of brain electrophysiology and behavior have been shown to be sensitive to even short periods of nutritional inadequacy.[4,5,6] As a result, nutrition may be an important modifiable lifestyle factor in age-related cognitive decline.

Key Nutrients for Brain Health

The link between nutrition and cognitive performance stems from the knowledge that the central nervous system (CNS) relies on a constant supply of glucose and nearly all of the essential nutrients for effective functioning.[7] A proper diet in the form of adequate protein, minerals, and vitamins is also required for full muscle function.

While overt vitamin deficiencies are uncommon—even among the elderly—subclinical vitamin deficiencies have been shown to play a role in the pathogenesis of declining neurocognitive function in aging.

Figure 1. Neurological and behavioural effects of vitamin deficiencies[8]

Vitamin	Presentation
Thiamin	Beri-Beri, Wernicke-Korsakoff's psychosis
Niacin	Pellagra, demetia
Pantothenic Acid	Myelin degeneration
Pyridoxine (B-6)	Peripheral neuropathy, convulsions
Folate	Irritability, depression, paranoia

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Cobalamin (B-12)	Peripheral neuropathy, subacute combined system degeneration, dementia
Vitamin E	Spinocerebellar degeneration, peripheral axonopathy

B Complex Vitamins

The B vitamins are of particular interest for brain health because subclinical deficiencies in these vitamins are relatively common in the general population and specifically among older adults, who may have a reduced ability to absorb both folate and protein-bound vitamin B12 due to age-related changes in the gastrointestinal tract and/or vitamin metabolism.[8] Recent cross-sectional and longitudinal studies have provided evidence for an association between B vitamins and several aspects of cognitive performance, with prior intake of B vitamins serving as a predictor of cognitive status at a later date.[9]

Folate and vitamin B12 (cobalamin) play fundamental roles in CNS function at all ages, including nucleotide and DNA synthesis and tissue growth, differentiation, and repair. Deficiencies in these B vitamins may lead to neurological and neuropsychiatric disorders. Methylcobalamin, the form of vitamin B12 that is active in the CNS, is a necessary cofactor for the conversion of homocysteine to methionine, so vitamin B12 deficiency contributes to the accumulation of homocysteine.

Population studies have demonstrated that, regardless of vitamin B status, plasma homocysteine concentrations increase with age.[10] Low folate and high homocysteine levels are associated with cognitive impairment, Alzheimer's disease, vascular dementia, and depression.[11,12,13,14] Although clinical vitamin B12 deficiency is relatively rare, mild, subclinical deficiency is present in an estimated 3.2 percent of adults aged 51 and older.[15] Research has shown that lower levels of folate and vitamin B12—even within the normal range—may interact to produce CNS metabolic abnormalities affecting cognitive function.[16]

Folate supplementation in older adults with low plasma folate levels and mild to moderate memory complaints has been shown to improve attention and memory, with the greatest cognitive improvements found in those with greater folate deficiency.[17] High-dose vitamin B treatment (folic acid 0.8 mg, vitamin B6 20 mg, and vitamin B12 0.5 mg) has been shown to lower plasma homocysteine levels and slow shrinkage of whole brain volume over two years among patients with baseline elevated plasma homocysteine levels.[18] It has also been shown to reduce—by as much as seven-fold—cerebral atrophy in the gray matter regions most vulnerable to the Alzheimer's disease process, including the medial temporal lobe, among elderly people with mild cognitive impairment and high homocysteine levels.[19]

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Vitamin E

The brain is highly susceptible to damage associated with oxidative stress caused by free radicals, which increases with aging and leads to neurodegeneration.[20] Oxidative stress, inflammation, and increased cholesterol levels are all mechanisms that have been linked to Alzheimer's disease pathology. Vitamin E includes a group of eight structurally related, lipid-soluble, chain-breaking antioxidants—four tocopherols and four tocotrienols—that act as free radical scavengers.

Alpha-tocopherol is the most abundant and bioavailable antioxidant form of vitamin E in human tissues. [21]

Due its antioxidant properties, vitamin E has been investigated as a treatment to ameliorate the cognitive decline that naturally occurs during aging, as well as to delay the onset or progression of Alzheimer's disease. Research has repeatedly associated high plasma vitamin E levels with better cognitive performance.[20] In one study of approximately 15,000 women aged 70-79 years, those who took a combination of vitamin E and C supplements for 20 years had better cognitive performance than those who did not. And, those women who had been taking vitamin E and C supplements for the longest were found to be 1.5 years younger by cognitive age.[22]

In addition, a reduced risk of developing Alzheimer's disease has been observed in individuals with high plasma levels of vitamin E and following vitamin E intake.[23,24] Among patients diagnosed with mild to moderate Alzheimer's disease, vitamin E supplementation has been associated with a significant delay in the clinical progression of symptoms and the deterioration of daily life activities, as well as a reduced need for care.[25,26] These data suggest that vitamin E supplementation of 2000 IU/day is safe and may be sufficient to delay the functional decline observed in Alzheimer's disease.

The biological relevance and neuroprotective properties of vitamin E may extend beyond its antioxidant activity. More recently, vitamin E has been shown to play a critical role in signaling, membrane fluidity, and gene regulation.[20] Animal studies have shown that low alpha-tocopherol levels in the brain induce downregulation of genes involved in myelination, neuronal vesicle transport, and glial functions.[27] They have also shown that the expression of a number of genes linked to the onset and progression of Alzheimer's disease is vitamin E-responsive.[28]

Other Nutrients

- Vitamin A—Vitamin A is the parent compound of the retinoids. There is an increasing body of evidence that retinoid signaling plays an important role in the function of the mature brain. These retinoid signalling pathways have been implicated in the pathophysiology

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of Alzheimer's disease, suggesting that adequate nutritional vitamin A status is important for adult brain function.[29]

- Vitamin D—Over the last decade, the role of vitamin D in healthy brain development and function has been gaining support. Multiple lines of evidence suggest that vitamin D is a neuroactive steroid that leads to alterations in brain neurochemistry and adult brain function. Adult deficiencies of vitamin D have been associated with a variety of adverse CNS outcomes, including Alzheimer's disease, Parkinson's disease, and cognitive decline.

- Vitamin K—An emerging nutrient in brain function, vitamin K participates in the synthesis of sphingolipids, which are present in high concentrations in brain cell membranes. In recent years, studies have linked alterations in sphingolipid metabolism to age-related cognitive decline and neurodegenerative diseases, such as Alzheimer's disease.[30]

- Boron—Although the trace element boron has yet to be recognized as an essential nutrient, data from animal and human studies suggest that boron may be important for cell membrane function, mineral and hormone metabolism, and enzyme reactions.[31] Studies of healthy older men an women have shown that even relatively short periods of restricted dietary boron intake can have a negative impact on brain function and various cognitive and psychomotor tasks.[32,33] When compared to older adults with a dietary boron intake of approximately 3.25 mg/day, older adults with a dietary boron intake of 0.25 mg/day exhibited increased low-frequency electroencephalogram (EEG) activity, which is linked to reduced mental alertness, impaired memory and poorer performance on vigilance and psychomotor tasks. Restricted dietary boron intake was also associated with significantly poorer performance on tasks emphasizing manual dexterity, hand-eye coordination, attention, perception, short-term memory, and long-term memory.[34]

  Average daily intake of boron from food sources ranges between 1.7 and 7 milligrams per day.[35] The recommended dietary allowance has not been established, but no toxicity has been identified and supplementation with up to one to three milligrams of boron per day is considered to be safe, as the upper intake level set by the Institute of Medicine for adults is 20 mg/day.[36]

- Zinc—Zinc acts as a neuromodulator at excitatory synapses and plays a significant role in the stress response and in the function of zinc-dependent enzymes that contribute to maintaining brain compensatory capacity. Alterations in zinc homeostasis have been reported in both Parkinson's and Alzheimer's disease, as well as in seizures and traumatic brain injury. There is also a growing body of evidence that age-related changes to the brain—frequently associated with a decline in brain function and impaired cognitive performance—could be related to dysfunctions affecting intracellular zinc ion availability.

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Zinc supplementation may be useful for preventing age-related urodegenerative disorders, as well as for preserving overall health in the context of zinc deficiency, which is common among the elderly.[37,38] Dietary supplementation with physiological doses of zinc restores deranged immune-endocrine functions in aging and enhances resistance to infections in the elderly, but to date, the full impact of zinc supplementation on brain function is yet to be determined.[39] What is certain is that a narrow range of zinc ions is beneficial for cell functions and high zinc ion concentrations can be toxic. As such, the effect of zinc supplementation is strictly dependent on the dose and length of treatment. Studies have shown a beneficial effect of supplementation with 15 mg/day of zinc over a period of 1-7 months, in association with other micronutrients, on the cognitive functions of elderly individuals.[40]

Nutritional Supplementation for Healthy Brain Function

A growing body of evidence supports the view that continued physical activity and good nutritional status are important determinants of physical and cognitive function as we age. And, improving diet and nutrition may help to prevent or reverse at least some of the cognitive decline associated with aging.[8]

Data from the National Health and Nutrition Examination Survey show that intakes of vitamins A, C, D, E, K, and folate are low in a significant proportion of the elderly population in the U.S.[41] Nutritional deficiencies among older adults may be due to a reduced capacity for self-care and nutrition or decreased nutrient absorption, metabolism, storage, and utilization. There is growing interest in the development of nutritional supplements as therapeutic agents aimed at maintaining or even enhancing cognitive function and slowing cognitive decline.

Forté Elements Brain Supplement

Formulated by licensed physicians, the Forté Elements Brain supplement is specifically designed to support healthy brain function and help delay or prevent age-related cognitive decline. Unlike other dietary supplements marketed for brain health, the Forté Elements Brain supplement is a Mediceutical, an emerging category of nutritional support that meets stringent standards of manufacture and evidence-based research. A pioneer in the Mediceutical industry, Forté

Supplement Facts

Serving Size 1 Pack (2 Capsules)
Servings Per Container 60

Amount Per Serving	% Daily Value*
Vitamin A (Beta-Carotene and Acetate) 1750 IU	35%
Vitamin C (Calcium Ascorbate) 450mg	750%
Vitamin D (Cholecalciferol) 200 IU	50%
Vitamin E (d-Alpha Tocopheryl) 25 IU	83%
Vitamin K (Fat Soluble) 12.5mcg	16%
Thiamin (Vitamin B1) 750mcg	50%
Riboflavin (Vitamin B2) 850mcg	50%
Niacin (Vitamin B3) 10mg	50%
Vitamin B6 (Pyridoxine) 10mg	500%
Folic Acid 400mcg	100%
Vitamin B12 (Cyanocobalamin) 250mcg	4167%
Biotin 15mcg	5%
Pantothenic Acid 5mg	50%
Calcium (as Carbonate & Ascorbate) 100mg	10%
Iron (Fumarate) 5mg	28%
Phosphorus (Potassium Phosphate) 50mg	5%
Iodine 75mcg	50%
Magnesium (Hydroxide) 50mg	25%
Zinc (Sulfate) 7.5mg	50%
Selenium 10mcg	14%
Copper (Sulfate) 1mg	50%
Manganese (Sulfate) 1mg	50%
Chromium (Polynicotinate) 10mcg	8%
Potassium (Potassium Phosphate) 60mg	2%
Boron 75mcg	**

*Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs.
**Daily Value not established.

OTHER INGREDIENTS: GELATIN(CAPSULE), MAGNESIUM STEARATE AND SILICA
CONTAINS: FISH

WARNING: ACCIDENTAL OVERDOSE OF IRON-CONTAINING PRODUCTS IS A LEADING CAUSE OF FATAL POISONING IN CHILDREN UNDER 6. KEEP THIS PRODUCT OUT OF REACH OF CHILDREN. IN CASE OF ACCIDENTAL OVERDOSE, CALL A DOCTOR OR POISON CONTROL CENTER IMMEDIATELY.

Supplement Facts

Serving Size 2 Softgel
Servings Per Container 60

Amount Per Serving	% Daily Value*
Calories 20	1%
Calories from Fat 20	
Total Fat 2g	3%
Polyunsaturated Fat 0.5g	**
Vitamin E 1.1 IU (d-Alpha Tocopherol plus d-Alpha, d-Beta, d-Gamma, & d-Delta)	4%
Fish Oil 2,000mg	**
EPA (Eicosapentaenoic Acid) 360mg	**
DHA (Docosahexaenoic Acid) 240mg	**

*Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs.
**Daily Value not established.

OTHER INGREDIENTS: GELATIN AND GLYCERIN

THIS STATEMENT HAS NOT BEEN EVALUATED BY THE FDA. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT, CURE, OR PREVENT ANY DISEASE

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Elements has defined strict criteria for its nutrient supplementation systems. In order to be categorized as a Mediceutical, a supplement must:

1. Be formulated to support a specific health condition or situation
2. Contain only non-synthetic, pharmaceutical-grade ingredients that are Generally Recognized as Safe (GRAS)
3. Contain elements that have been validated by clinical research for the specific health condition or situation, as published in peer-reviewed journals
4. Conform to pharmaceutical-grade dosage standards for the specific health condition or situation
5. Be produced in FDA-compliant manufacturing facilities using pharmaceutical-grade manufacturing practices
6. Be accompanied by a Certificate of Analysis confirming that product ingredients meet the mediceutical standard and are as listed on the product label

These rigorous guidelines ensure that all Forté Elements mediceutical supplements offer the right blend of nutrients at the right dose for the specific clinical condition. In the case of brain health, the Forté Elements Brain Capsule contains key vitamins and trace minerals that have been shown to play a role in healthy brain function, at dosages that have been deemed safe for long-term use.

With increasing longevity, the need to maintain functional well-being, especially cognitive function, is a major determinant of the quality of life in older age.[8] In 2005, the worldwide incidence of dementia was approximately 24 million and, by 2050, the global prevalence of dementia is expected to quadruple.[42] In the U.S., costs associated with Alzheimer's disease were estimated to be around $203 billion in 2013.[43] Nutritional support may help to preserve brain compensatory capacity, prevent the onset of neurodegenerative diseases, and reduce healthcare costs related to diminished cognition.

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A fusion of science and practical medical experience unlike anything that has come before.

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